

## **I. REMARKS**

### **A. Status of the Claims**

Claims 1 through 9 and 52 are pending.

Claims 10 through 29 and 32 through 51 have been canceled.

Claims 1 through 9 and 52 are rejected.

### **B. Rejection Under § 102(b)**

Claims 1 and 52 are rejected under 35 U.S.C. § 102(b), as anticipated by US 4,950,432 to Mehta et al. ("Mehta '432"). This rejection is respectfully traversed.

Applicants' maintain the claim limitations are not process to be ignored by reason of being "process" limitations in composition claims. These limitations are product limitations cognizable as claim limitations defining the present invention. Particular emphasis is placed on the product defining characteristics of "aqueous/t-butanol solvent system," "facile-reconstitute" and "submicron-reconstitute"

Applicants respectfully submit that the Examiner improperly excludes such limitations on the basis that, in the Examiner' view, such limitations are process/use limitations not cognizable for apparatus claim definition. Applicants maintain that *In re Mattison and Swanson*, 184 U.S.P.Q. 484, 485 (CCPA 1975) is controlling. The holding in *Mattison* was to § 112, second paragraph, definiteness. Applicants submit that, if definite under § 112, second paragraph, the claim language is necessarily limiting of the claims. In the previous Amendment and Response Submitted June 17, 1999, Applicants argued that the 35 USC § 112, second paragraph, rejection of the terms "facile-reconstitute" and "submicron-reconstitute as indefinite was improper. This

basis of rejection was dropped. As definite terms, the limitations represented by these terms is submitted as cognizable.

Reference is made to *In re Finsterwalder* 168 USPQ 530 (CCPA 1971). In, *Finsterwalder*, the court evaluated arguably process connoting phrases as “torsionally rigid” and “a number of cross-bearers which extend out on both sides from said girders and are moveable therewith.” *Finsterwalder* accepts the dynamic aspect of “moveable therewith” as a limitation to be given weight in defining the claimed structure. *Finsterwalder*, at 534. Thus, *Finsterwalder* holds that an active aspect of a claimed apparatus that defines the apparatus shall be given weight in distinguishing the claimed subject matter over prior art.

Applicants’ composition -- a defined lyophilate -- stands in the same position as the apparatus of *Finsterwalder*. The limitations the Examiner deems to be process limitations are respectfully submitted to reflect limitations of language. By each such limitation, the invention is distinguished over the prior art.

With reference to submicron liposomes which appear upon reconstitution, attention is drawn to Specification page 8, lines 23 and 26, page 19, line 25 through page 20, line 21, and Figs 2 and 3.

The superiority of facile reconstitution -- a physical property of the lyophilate -- is stated at page 19, lines 16-20 and page 20, lines 21-23.

As to solvent systems, the claimed aqueous/t-butanol is clearly a cognizable limitation in the product-by-process mode.

Mehta ‘432 does not yield submicron liposomes, nor is it facile reconstitute, nor does it meet the definition of aqueous/t-butanol solvent-system defining the absence of trace organic solvents.

The rejection under Mehta '432 relies solely on the discounting of Applicants' claimed limitations as being process limitations not cognizable in a composition of matter claim. It is respectfully submitted that the claim limitations are properly considered and may not be ignored.

The Examiner's remarks that the Applicants' arguments related to "heating to 40 degrees and filtering" are particular traversed. (Office Action of September 9, 1999, page 3, top). Applicants' previous response (June 17, 1999, page 10, first paragraph) makes reference 40° C in illuminating the difficulty Mehta '432 discloses in reconstituting the lyophilate of Mehta '432. This was one fact establishing that Mehta '432 did not disclose a facile reconstitute product. In distinction, Applicants' claimed facile-reconstitute lyophilate will fully reconstitute with hand-shaking in about 1 minute, to obtain liposomes of about 400nm or less. Applicants' product as claimed is distinct from that of Mehta '432 and does not require insertion of the a reference to temperature to be distinct.

As to Claim 52, dependent on Claim 1, the limitation of halogenated solvent-free is noted. Mehta '432 uses halogenated solvents (*e.g.*, Mehta '432, col. 5, lines 42-45, methylene chloride; col. 6, line 5-8, chloroform). Removal is by evaporation, (col. 6, lines 11-14). This does not yield the halogenated solvent-free lyophilate as defined by Applicants.

Mehta '432 does not anticipate either Claim 1 or Claim 52 with all limitations. It is respectfully requested that this rejection be withdrawn.

**C. Rejection Under § 102(e)**

Claims 1, and 52 are rejected under 35 U.S.C. § 102(e), as anticipated by US 5,811,119 to Mehta et al. ("Mehta '119"). This rejection is respectfully traversed.

The rejection under Mehta '119, as with Mehta '432, is not supported when read in view of Applicants' claimed limitations as to either Claim 1 or Claim 52. The limitations are as to solvent system, reconstitution and size upon reconstitution are cognizable in the present composition of matter claim.

Mehta '119 does not anticipate either Claim 1 or Claim 52 with all limitations. It is respectfully requested that this rejection be withdrawn.

**D. Rejection Under § 103(a)**

Claims 2 through 9 are rejected under 35 U.S.C. § 103(a), as obvious in view of either Mehta '432 or Mehta '119 as cited above and further in view of US 5,585,12 to Unger ("Unger"), US 5,089,602 to Isliker (Isliker) and US 5,653,996 to Hsu ("Hsu") individually or in combination. This rejection is respectfully traversed.

As noted by the Examiner, the present rejection is based on disregarding Applicants' claim limitations deemed to be process limitations inapplicable to a composition of matter claim. Applicants' reiterate the argument presented above that the limitations are as to solvent system, reconstitution, and size upon reconstitution are cognizable in the present composition of matter claim, as supported by case law. In view of this, the present rejection is unsupported and respectfully submitted to be improper.

As noted by the Examiner, Mehta ['432 and '119] fails to disclose surfactants such as Tweens. Mehta '432 & '119 also fails to disclose the specific solvent system, the ease of reconstitution, and the submicron product upon reconstitution. None of Unger, Isliker, or Hsu supply these deficiencies.

The Examiner's rejection is particularly dependent on Unger in combination with Mehta. Office Action of September 9, 1999, page 5, top. In view of the deficiencies of either Mehta reference when all of Applicants' claim limitations are considered, Unger cannot render the present invention obvious.

Applicants claim a submicron facile-reconstitute preliposomal powder derived from an aqueous/t-butanol solvent system. Unger does not teach or suggest any of these conditions. Unger does not mention t-butanol. Unger teaches away from the sub-micron condition in specifying that only larger liposomes were produced when detergent was employed. Unger teaches only lengthy vortex reconstitution of detergent containing liposomes.

It is reemphasized that Unger, as to surfactant-containing liposomes, is explicit that "the smallest size detected is about 6  $\mu\text{m}$  -- without regard to surfactant concentration. Applicants' claimed submicron liposomes are distinct. The teaching of Unger on reconstitution is that vortexing for 10 minutes is required. The teaching of Unger is that the use of surfactants and lyophilization leads to large liposomes with vortexing required for reconstitution is a teaching away from the present invention. The combination of Unger with either Mehta '432 or Mehta '119, as taught by Unger, will not lead to a lyophilate that is facile-reconstitute or which will produce submicron liposomes. This is contrary to that which is claimed.

Neither Unger, nor Isliker nor Hsu discloses the claimed solvent system.

Isliker does not teach or suggest the use of Tween or any other surfactant except as found within an intermediate processing step. Neither facile-reconstitute liposomes nor submicron liposomes are taught or suggested by Isliker. Nothing in Isliker supplies any deficiency of Mehta '432, Mehta '119 or Unger. The present invention cannot be rendered obvious by this combination of references.

As to Hsu, Hsu does not supply the deficiencies of either Mehta patent to the claimed sub-micron, facile-reconstitute preliposomal powder derived from an aqueous/t-butanol solvent system. Hsu suggests no more than that Tweens can be employed in liposomal preparation. Even if applied to the Mehta patents, no combination of Mehta '432 or Mehta '119 with any or all of Unger, Isliker, or Hsu arrive at the claimed invention.

In specific, Claim 3 is drawn to a preliposomal lyophilate containing anionic, cationic or nonionic surfactant. Unger teaches away from such surfactants for imparting the claimed submicron liposome size and ease of reconstitution. Isliker fails to disclose detergent containing lyophilate. And Hsu offers is no more than a surfactant without solvent system or any reason to combine the necessary elements, and neither Mehta can provide for such deficiencies.

Claim 4, specifies nonionic surfactant, and Unger, Isliker or Hsu can no more provide these elements to Mehta '432 or Mehta '119 than they could to Claim 3.

Claim 5 which specifies Tween as the surfactant; Claim 6 which specifies Tween 20, and Claim 7, 8 and 9 offer particular amounts of surfactant. Unger teaches away from and is inconsistent with the claimed invention. Isliker and Hsu offer no amounts of the surfactant to provide the claimed invention.

None of the five cited references alone or in combination render the instant invention obvious.

## II. CONCLUSION

Allowance of the present claims is requested.

Respectfully submitted,



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